MAY 2 6 2000 8

SEQUENCE LISTING

Wands, Jack R. de la Monte, Suzanne M. Ince, Nedim Carlson, Rolf I.

<120> DIAGNOSIS AND TREATMENT OF MALIGNANT NEOPLASMS

<130> R.I. Hosp. - Malignant Neoplasms

<140> USSN 09/436,184

<141> 1999-11-08

<160> 7

<170> PatentIn Ver. 2.0

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<211> 36

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Consensus EGF-like domain

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<223> Wherein any Xaa may be any amino acid

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Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Xaa Cys Xaa Xaa Xaa Xaa Xaa Xaa 20 25 30

Xaa Xaa Xaa Cys

35

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<211> 758

<212> PRT

<213> Homo sapiens

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Gly Ser Gly Ser Thr Ser Ala Gly Ser Ser Pro Gly Ala
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Arg Arg Glu Thr Lys His Gly Gly His Lys Asn Gly Arg Lys Gly Gly
35 40 45

Leu Ser Gly Thr Ser Phe Phe Thr Trp Phe Met Val Ile Ala Leu Leu 50 55 60

Gly Val Trp Thr Ser Val Ala Val Val Trp Phe Asp Leu Val Asp Tyr 65 70 75 80

Glu Glu Val Leu Gly Lys Leu Gly Ile Tyr Asp Ala Asp Gly Asp Gly 85 90 95

Asp Phe Asp Val Asp Asp Ala Lys Val Leu Leu Gly Leu Lys Glu Arg
100 105 110

Ser Thr Ser Glu Pro Ala Val Pro Pro Glu Glu Ala Glu Pro His Thr 115 120 125

Glu Pro Glu Glu Gln Val Pro Val Glu Ala Glu Pro Gln Asn Ile Glu 130 135 140

Asp Glu Ala Lys Glu Gln Ile Gln Ser Leu Leu His Glu Met Val His 145 150 155 160

Ala Glu His Val Glu Gly Glu Asp Leu Gln Gln Glu Asp Gly Pro Thr 165 170 175

Gly Glu Pro Gln Gln Glu Asp Asp Glu Phe Leu Met Ala Thr Asp Val 180 185 190

Asp Asp Arg Phe Glu Thr Leu Glu Pro Glu Val Ser His Glu Glu Thr
195 200 205

Glu His Ser Tyr His Val Glu Glu Thr Val Ser Gln Asp Cys Asn Gln 210 215 220

Asp Met Glu Glu Met Met Ser Glu Gln Glu Asn Pro Asp Ser Ser Glu 225 230 235 240

Pro Val Val Glu Asp Glu Arg Leu His His Asp Thr Asp Asp Val Thr
245 250 255

Tyr Gln Val Tyr Glu Glu Gln Ala Val Tyr Glu Pro Leu Glu Asn Glu

260 265 270

Gly Ile Glu Ile Thr Glu Val Thr Ala Pro Pro Glu Asp Asn Pro Val Glu Asp Ser Gln Val Ile Val Glu Glu Val Ser Ile Phe Pro Val Glu Glu Gln Gln Glu Val Pro Pro Glu Thr Asn Arg Lys Thr Asp Asp Pro Glu Gln Lys Ala Lys Val Lys Lys Lys Pro Lys Leu Leu Asn Lys Phe Asp Lys Thr Ile Lys Ala Glu Leu Asp Ala Ala Glu Lys Leu Arg Lys Arg Gly Lys Ile Glu Glu Ala Val Asn Ala Phe Lys Glu Leu Val Arg Lys Tyr Pro Gln Ser Pro Arg Ala Arg Tyr Gly Lys Ala Gln Cys Glu Asp Asp Leu Ala Glu Lys Arg Arg Ser Asn Glu Val Leu Arg Gly Ala Ile Glu Thr Tyr Gln Glu Val Ala Ser Leu Pro Asp Val Pro Ala Asp Leu Leu Lys Leu Ser Leu Lys Arg Arg Ser Asp Arg Gln Gln Phe Leu Gly His Met Arg Gly Ser Leu Leu Thr Leu Gln Arg Leu Val Gln Leu Phe Pro Asn Asp Thr Ser Leu Lys Asn Asp Leu Gly Val Gly Tyr Leu Leu Ile Gly Asp Asn Asp Asn Ala Lys Lys Val Tyr Glu Glu Val Leu Ser Val Thr Pro Asn Asp Gly Phe Ala Lys Val His Tyr Gly Phe Ile Leu Lys Ala Gln Asn Lys Ile Ala Glu Ser Ile Pro Tyr Leu Lys

Glu Gly Ile Glu Ser Gly Asp Pro Gly Thr Asp Asp Gly Arg Phe Tyr

515 520 525

Phe His Leu Gly Asp Ala Met Gln Arg Val Gly Asn Lys Glu Ala Tyr 530 540

Lys Trp Tyr Glu Leu Gly His Lys Arg Gly His Phe Ala Ser Val Trp 545 550 555 560

Gln Arg Ser Leu Tyr Asn Val Asn Gly Leu Lys Ala Gln Pro Trp Trp 565 570 575

Thr Pro Lys Glu Thr Gly Tyr Thr Glu Leu Val Lys Ser Leu Glu Arg
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Asn Trp Lys Leu Ile Arg Asp Glu Gly Leu Ala Val Met Asp Lys Ala 595 600 605

Lys Gly Leu Phe Leu Pro Glu Asp Glu Asn Leu Arg Glu Lys Gly Asp 610 620

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Cys Lys Gly Ala Pro Lys Thr Cys Thr Leu Leu Glu Lys Phe Pro Glu 645 650 655

Thr Thr Gly Cys Arg Arg Gly Gln Ile Lys Tyr Ser Ile Met His Pro 660 665 670

Gly Thr His Val Trp Pro His Thr Gly Pro Thr Asn Cys Arg Leu Arg 675 680 685

Met His Leu Gly Leu Val Ile Pro Lys Glu Gly Cys Lys Ile Arg Cys 690 695 700

Ala Asn Glu Thr Arg Thr Trp Glu Glu Gly Lys Val Leu Ile Phe Asp 705 710 715 720

Asp Ser Phe Glu His Glu Val Trp Gln Asp Ala Ser Ser Phe Arg Leu 725 730 735

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<210> 4 <211> 31 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence: EGF-like cysteine-rich repeat <220> <223> Wherein any Xaa may be any amino acid Cys Asp Xaa Xaa Cys Xaa Xaa Lys Xaa Gly Asn Gly Xaa Cys Asp 5 Xaa Xaa Cys Asn Asn Ala Ala Cys Xaa Xaa Asp Gly Xaa Asp Cys 20 25 30 <210> 5 <211> 1242 <212> PRT <213> Homo sapiens <400> 5 Met Ala Ser Pro Pro Glu Ser Asp Gly Phe Ser Asp Val Arg Lys Val Gly Tyr Leu Arg Lys Pro Lys Ser Met His Lys Arg Phe Phe Val Leu 20 Arg Ala Ala Ser Glu Ala Gly Gly Pro Ala Arg Leu Glu Tyr Tyr Glu 40 Asn Glu Lys Lys Trp Arg His Lys Ser Ser Ala Pro Lys Arg Ser Ile 55 Pro Leu Glu Ser Cys Phe Asn Ile Asn Lys Arg Ala Asp Ser Lys Asn 65 70 75 Lys His Leu Val Ala Leu Tyr Thr Arg Asp Glu His Phe Ala Ile Ala 85 90 95 Ala Asp Ser Glu Ala Glu Gln Asp Ser Trp Tyr Gln Ala Leu Leu Gln 100 105 110

Leu His Asn Arg Ala Lys Gly His His Asp Gly Ala Ala Ala Leu Gly

125

120

115

Ala Gly Gly Gly Gly Ser Cys Ser Gly Ser Ser Gly Leu Gly Glu Ala Gly Glu Asp Leu Ser Tyr Gly Asp Val Pro Pro Gly Pro Ala Phe Lys Glu Val Trp Gln Val Ile Leu Lys Pro Lys Gly Leu Gly Gln Thr Lys Asn Leu Ile Gly Ile Tyr Arg Leu Cys Leu Thr Ser Lys Thr Ile Ser Phe Val Lys Leu Asn Ser Glu Ala Ala Val Val Leu Gln Leu Met Asn Ile Arg Arg Cys Gly His Ser Glu Asn Phe Phe Ile Glu Val Gly Arg Ser Ala Val Thr Gly Pro Gly Glu Phe Trp Met Gln Val Asp Asp Ser Val Val Ala Gln Asn Met His Glu Thr Ile Leu Glu Ala Met Arg Ala Met Ser Asp Glu Phe Arg Pro Arg Ser Lys Ser Gln Ser Ser Ser Asn Cys Ser Asn Pro Ile Ser Val Pro Leu Arg Arg His His Leu Asn Asn Pro Pro Pro Ser Gln Val Gly Leu Thr Arg Arg Ser Arg Thr Glu Ser Ile Thr Ala Thr Ser Pro Ala Ser Met Val Gly Gly Lys Pro Gly Ser Phe Arg Val Arg Ala Ser Ser Asp Gly Glu Gly Thr Met

Arg Thr His Ala His Arg His Arg Gly Ser Ala Arg Leu His Pro Pro

Leu Asn His Ser Arg Ser Ile Pro Met Pro Ala Ser Arg Cys Ser Pro

Ser Arg Pro Ala Ser Val Asp Gly Ser Pro Val Ser Pro Ser Thr Asn

Ser Ala Thr Ser Pro Val Ser Leu Ser Ser Ser Thr Ser Gly His Gly Ser Thr Ser Asp Cys Leu Phe Pro Arg Arg Ser Ser Ala Ser Val Ser Gly Ser Pro Ser Asp Gly Gly Phe Ile Ser Ser Asp Glu Tyr Gly Ser Ser Pro Cys Asp Phe Arg Ser Ser Phe Arg Ser Val Thr Pro Asp Ser Leu Gly His Thr Pro Pro Ala Arg Gly Glu Glu Leu Ser Asn Tyr Ile Cys Met Gly Gly Lys Gly Pro Ser Thr Leu Thr Ala Pro Asn Gly His Tyr Ile Leu Ser Arg Gly Gly Asn Gly His Arg Cys Thr Pro Gly Thr Gly Leu Gly Thr Ser Pro Ala Leu Ala Gly Asp Glu Ala Ala Ser Ala Ala Asp Leu Asp Asn Arg Phe Arg Lys Arg Thr His Ser Ala Gly Thr Ser Pro Thr Ile Thr His Gln Lys Thr Pro Ser Gln Ser Ser Val Ala Ser Ile Glu Glu Tyr Thr Glu Met Met Pro Ala Tyr Pro Pro Gly Gly Gly Ser Gly Gly Arg Leu Pro Gly His Arg His Ser Ala Phe Val Pro Thr Arg Ser Tyr Pro Glu Glu Gly Leu Glu Met His Pro Leu Glu Arg Arg Gly Gly His His Arg Pro Asp Ser Ser Thr Leu His Thr Asp Asp Gly Tyr Met Pro Met Ser Pro Gly Val Ala Pro Val Pro Ser Gly Arg Lys Gly Ser Gly Asp Tyr Met Pro Met Ser Pro Lys Ser Val

Ser Ala Pro Gln Gln Ile Ile Asn Pro Ile Arg Arg His Pro Gln Arg Val Asp Pro Asn Gly Tyr Met Met Ser Pro Ser Gly Gly Cys Ser Pro Asp Ile Gly Gly Pro Ser Ser Ser Ser Ser Ser Ser Asn Ala Val Pro Ser Gly Thr Ser Tyr Gly Lys Leu Trp Thr Asn Gly Val Gly Gly His His Ser His Val Leu Pro His Pro Lys Pro Pro Val Glu Ser Ser Gly Gly Lys Leu Leu Pro Cys Thr Gly Asp Tyr Met Asn Met Ser Pro Val Gly Asp Ser Asn Thr Ser Ser Pro Ser Asp Cys Tyr Tyr Gly Pro Glu Asp Pro Gln His Lys Pro Val Leu Ser Tyr Tyr Ser Leu Pro Arg Ser Phe Lys His Thr Gln Arg Pro Gly Glu Pro Glu Glu Gly Ala Arg His Gln His Leu Arg Leu Ser Thr Ser Ser Gly Arg Leu Leu Tyr Ala Ala Thr Ala Asp Asp Ser Ser Ser Ser Thr Ser Ser Asp Ser Leu Gly Gly Tyr Cys Gly Ala Arg Leu Glu Pro Ser Leu Pro His Pro His His Gln Val Leu Gln Pro His Leu Pro Arg Lys Val Asp Thr Ala Ala Gln Thr Asn Ser Arg Leu Ala Arg Pro Thr Arg Leu Ser Leu Gly Asp Pro Lys Ala Ser Thr Leu Pro Arg Ala Arg Glu Gln Gln Gln

Gln Gln Pro Leu Leu His Pro Pro Glu Pro Lys Ser Pro Gly Glu Tyr

Val Asn Ile Glu Phe Gly Ser Asp Gln Ser Gly Tyr Leu Ser Gly Pro 900 905 910

Val Ala Phe His Ser Ser Pro Ser Val Arg Cys Pro Ser Gln Leu Gln 915 920 925

Pro Ala Pro Arg Glu Glu Glu Thr Gly Thr Glu Glu Tyr Met Lys Met 930 935 940

Asp Leu Gly Pro Gly Arg Arg Ala Ala Trp Gln Glu Ser Thr Gly Val 945 950 955 960

Glu Met Gly Arg Leu Gly Pro Ala Pro Pro Gly Ala Ala Ser Ile Cys 965 970 975

Arg Pro Thr Arg Ala Val Pro Ser Ser Arg Gly Asp Tyr Met Thr Met 980 985 990

Gln Met Ser Cys Pro Arg Gln Ser Tyr Val Asp Thr Ser Pro Ala Ala 995 1000 1005

Pro Val Ser Tyr Ala Asp Met Arg Thr Gly Ile Ala Ala Glu Glu Val 1010 1015 1020

Ser Leu Pro Arg Ala Thr Met Ala Ala Ala Ser Ser Ser Ser Ala Ala 1025 1030 1035 1040

Ser Ala Ser Pro Thr Gly Pro Gln Gly Ala Ala Glu Leu Ala Ala His 1045 1050 1055

Ser Ser Leu Leu Gly Gly Pro Gln Gly Pro Gly Gly Met Ser Ala Phe 1060 1065 1070

Thr Arg Val Asn Leu Ser Pro Asn Arg Asn Gln Ser Ala Lys Val Ile 1075 1080 1085

Arg Ala Asp Pro Gln Gly Cys Arg Arg His Ser Ser Glu Thr Phe 1090 1095 1100

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Ala Gly Ala Ala Val Gly Gly Gly Gly Ser Ser Ser Ser Glu 1125 1130 1135

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Ala Ala Gly Gly Leu Glu Asn Gly Leu Asn Tyr Ile Asp Leu Asp Leu 1170 1175 1180

Val Lys Asp Phe Lys Gln Cys Pro Gln Glu Cys Thr Pro Glu Pro Gln 1185 1190 1195 1200

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1